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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,777	05/23/2001	James W. Fett	10498-00012	2435

7590 06/27/2003

John P. Iwanicki
BANNER & WITCOFF, LTD.
28th Floor
28 State Street
Boston, MA 02109

EXAMINER
EPPS, JANET L

ART UNIT	PAPER NUMBER
1635	4

DATE MAILED: 06/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/863,777	FETT ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 24-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-9, 11, 13-14, 24-32* is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *10 and 12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-14-03 has been entered.

Claim Rejections - 35 USC § 112

2. Claims 1-9, 11 and 13 remain rejected, and claims 24-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the Official Action mailed 3-19-2002.

(a) Written Description Rejection: Applicant's arguments filed 4-14-03 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that "However, without acquiescing to the Examiner's rejections, Applicants have amended claim 1, 11, and 13 to recite a nucleic acid encoding human angiogenin thereby obviating the Examiner's rejection."

However, contrary to Applicant's assertions, although the instant claims have been amended to recite human angiogenin, it is noted that no specific structural information has been added to the claims so that the skilled artisan could precisely envision the structures of all compounds, comprising an oligonucleotide or analog thereof, that are useful for inhibiting the

expression of angiogenin, in particular wherein said compound is complementary to a "target portion" of a nucleic acid encoding human angiogenin. It remains that the instant claims encompass compounds, comprising oligonucleotides or analogs thereof, having a base sequence complementary to a "target portion" of a nucleic acid encoding all polymorphic, splice and allelic variants of human angiogenin. However, the antisense oligonucleotides described in the specification as filed, are designed based upon the structure of a single species of angiogenin nucleic acid sequence. Specifically, see Figure 1, wherein Applicants disclose the sequence of a nucleic acid sequence encoding human angiogenin.

Additionally, it is noted that in the first line of claim 1, 11, and 13, the claimed compounds are "for inhibiting expression of angiogenin" generically, however the compounds are designed to have a sequence complementary to human angiogenin nucleic acid. Applicants have not demonstrated that compounds complementary to human angiogenin nucleic acid have a defined structure correlated with the function of inhibiting the expression of all variants of angiogenin nucleic acid, for example.

Therefore, as stated in the prior office action, Applicant's disclosure combined with what is known in the prior art, are not sufficient to describe the claimed genus of compounds and compositions for inhibiting expression of all polymorphic, splice and allelic variants of human angiogenin.

In the instant case, Applicants are only in possession of antisense oligonucleotides targeting the nucleic acid sequence of human angiogenin as set forth in Figure 1 of the specification as filed. Further experimentation is required in order for applicant's to determine the sequence of all other polymorphic and allelic variants of angiogenin and furthermore identify

antisense oligonucleotides targeting these polymorphic and allelic variants of angiogenin nucleic acid.

(b) New Matter Rejection: Applicants have added claim 29, according to Applicants claim 29 was added to recite limitations that were deleted from claim 9. However, it is noted that there is no antecedent basis for the limitation "OCH3CH3" in either original claim 9 or in the specification as originally filed. Applicant is required to cancel the new matter in the reply to this Office Action. While an applicant is not limited to the nomenclature used in the application as filed, he or she should make appropriate amendment of the specification whenever this nomenclature is departed from by amendment of the claims so as to have clear support or antecedent basis in the specification for the new terms appearing in the claims. This is necessary in order to insure certainty in construing the claims in the light of the specification. See MPEP § 608.01(o)

3. Claims 5, 9, and 13-14, and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 recites "[T]he compound of claim 4 wherein the modified internucleotide linkage is selected from the group consisting of phosphorothioate...phosphodiester.." Claim 5 is vague and indefinite to the extent that the "modified internucleotide linkage" recited in this claim encompasses a "phosphodiester" linkage. The phosphodiester linkage is the naturally occurring internucleotide linkage that is present in a nucleic acid molecule. Therefore, if the internucleotide linkage is a "phosphodiester" linkage, it is not a modified linkage.

Additionally, claim 5 recites wherein the internucleotide linkage consists of "CH_3-O-$N(CH_3)$-CH_2." In regards to the CH_3-O moiety at the beginning of this linkage, it is unclear how the CH_3 group would form an internucleotide linkage since the "C" atom has utilized all of the free electrons available to make covalent bonds with other atoms. It is possible that Applicants intended this internucleotide linkage to consists of "CH_2-O-$N(CH_3)$-CH_2."

Claim 9 recites the phrase "substituted silyl: an RNA cleaving group: a cholesteryl group..." This phrase is vague and indefinite since, due to the presence of the colon (:) after the term "silyl," it appears that Applicants are attempting to define the term "substituted silyl." However, one of skill in the art would immediately recognize that a substituted silyl group is not an RNA cleaving group.

Claims 13-14 recite wherein the 2' position of a sugar ring is substituted with, for example, "-OCH_3OCH_3" or "$OCH_3O(CH_2)$p", however these terms are chemically improper, the correct terms are likely to be "OCH_2OCH_3," or "$OCH_2O(CH_2)$p."

Claim 29 recites the limitations "-OCH_3CH_3" and "$OCH_3O(CH_2)nCH_3$," however these terms are chemically improper, the correct terms are likely to be "OCH_2CH_3," or "$OCH_2O(CH_2)nCH_3$." Additionally, claim 29 recites wherein the modified 2' hydroxyl moiety is selected from the group consisting of "OH." This phrase is vague and indefinite since a hydroxyl group is not a modified 2' hydroxyl moiety.

Claim Rejections - 35 USC § 103

4. Claims 1-9, 11 and 13 remain rejected, and claims 24-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vallee et al., in view of Olson et al., Milligan et al., Burch, Anderson et al., and Artavanis-Tsakonas et al. for the reasons of record set forth in the Official Action mailed 3-19-2002.

Applicant's arguments filed 4-14-03 have been fully considered but they are not persuasive. Applicants argue that the primary reference of Vallee et al. does not teach or suggest an antisense approach to inhibiting expression of angiogenin. Applicants argue that the reference of Olson et al., does not provide motivation to look to an antisense approach to inhibit the expression of angiogenin. In regards to the Milligan et al. reference, Applicants argue that Milligan et al. is limited to speculation of the potential of antisense approaches in general, and that at best the combined reference provides only an "obvious-to-try" situation which is not the standard for obviousness.

However, contrary to Applicant's assertions, the prior art clearly provides motivation for exploring the role of human angiogenin expression in regulating tumor growth. As stated previously Olson teach that inhibition of angiogenin is an attractive therapeutic target for the treatment of both primary and metastatic cancer because angiogenesis is crucial in growth and metastatic spread of cancer. Furthermore, Olson et al. teach the use of antibodies to inhibit the expression of angiogenin. Milligan et al. provides a teaching that describes the use of antisense inhibitors to target the expression of a gene, wherein the antisense oligonucleotides can be designed in order to make potential specific therapeutic agents for any disease in which the causative gene is known, in the instant case the gene is angiogenin and the disease is primary and

metastatic cancer. In the instant case, in the absence of any evidence of unexpected results, it would have been obvious to substitute one potential inhibitor of angiogenin, in the instant case antisense oligonucleotides, for another (i.e. antibodies) in order to understand the role of this gene in the angiogenesis of tumors and for designing potential therapeutics for treating cancer by the design of antisense oligonucleotides targeting the expression of this gene.

One of ordinary skill in the art would have been motivated to further elucidate the function of angiogenin by inhibiting angiogenin gene expression because Olson et al., which does not explicitly teach antisense oligonucleotides that target angiogenin, does suggest inhibiting angiogenin in order to assess the role of angiogenin in tumor growth. Thus what was known particularly about angiogenin and tumor growth, as taught by the references of Vallee et al. and Olson et al., combined with the teaching of Milligan et al. for employing the antisense art, and the disclosures of Burch, Artavanis-Tsakonas et al., and Anderson for modifying oligonucleotides in general, render claims 1-9, 11, 13, and claims 24-32 unpatentable under 35 U.S.C. 103(a).

Claim Objections

5. Claims 10 and 12 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. Claim 14 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Fri, 8:30AM-6:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L. Epps-Ford, Ph.D.
Examiner
Art Unit 1635

JLE
June 24, 2003